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EXAMINER	
HOWARD, ZACHARY C	
ART UNIT	PAPER NUMBER
1646	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/581,468	BALASA ET AL.	
	Examiner	Art Unit	
	ZACHARY C. HOWARD	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-23* is/are pending in the application.

4a) Of the above claim(s) *21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-20,22 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *11-23* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 June 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/1/06;4/16/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 7/23/08 has been entered in full. Claims 1-10 are canceled. Claims 13, 18 and 20 are amended. New claims 22 and 23 are added.

Claims 11-23 are pending in the instant application.

Elections of Species

Applicants' elections of species in the reply filed on 7/23/08 are acknowledged.

(I) Applicants elect SEQ ID NO: 78 as the species of variable heavy chain.

Each of the pending claims is directed to the elected species as Applicants have canceled claims 1-10 that were directed to the non-elected species of SEQ ID NO: 50. This species election is currently rendered moot but will be necessarily reinstated if claims to the canceled subject are introduced in future claim amendments.

(II) Applicants elect Crohn's disease as the species of inflammatory bowel disease.

Claim 21 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim.

Claims 11-20, 22 and 23 are under consideration, as they read upon the elected species.

Drawings

The drawings are objected to for the following reasons. Figure 1A contains a sequence labeled T55I (representing a change of threonine to isoleucine at position 55), yet the sequence shown has a T59I mutation (i.e., the sequence shows a change of threonine to isoleucine at position 59). In the parent sequence HuAIP12, each of positions 55 and 59 has a threonine. In HuAIP13 and T55I, position 59 is changed to an isoleucine. Either the designation of "T55I" is wrong and should be "T59I", or the wrong threonine residue has been changed to I in the HuAIP13 and T55I sequences shown in

the Figure 1A. It is noted that in the Sequence Listing filed 6/1/06 that SEQ ID NO: 78 (indicated as T55I) has a threonine at position 55 and an isoleucine at position 59.

Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as “amended.” If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either “Replacement Sheet” or “New Sheet” pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

The disclosure is objected to because of the following informalities:

(1) An updated priority statement of the instant application’s parent provisional and nonprovisional applications should be included in the first sentence of the specification or application data sheet. Specifically, this information should indicate that the instant application is a 371 of PCT/US04/37600, filed 11/10/2004, which claims benefit of provisional application 60/527,882, filed on 12/4/2003.

(2) Page 3, lines 17-18 state, "...a variable light chain amino acid sequence of SEQ ID NO. 48, designated herein as the HuAIP12 T551 variant". However, on page 45, lines 17-19, the T55I variant is described as being made from the VH chain of HuAIP12. Figure 1A appears to support this by showing T55I as a VH sequence.

(3) In two instances, the specification incorrectly refers to the T55I variant (representing a change of threonine to isoleucine) as "T551" (using the number 1 instead of the letter I). These are located at page 3, line 18 and page 4, line 4.

(4) The Brief Description of Figure 1A states that it depicts "the HuAIP12 VH amino acid sequence (SEQ ID NO. 50), the HuAIP13 VH amino acid sequence (SEQ ID NO. 18), the HuAIP12 T55I variant VH amino acid sequence (SEQ ID NO. 78) and the HuAIP12 G104A variant VH amino acid sequence (SEQ ID NO. 79)" (pg 3, lines 30-33). Figure 1A shows four VH sequences labeled HuAIP12, HuAIP13, T55I and G104A, each of which is 119 amino acids. The Sequence Listing filed 6/1/06 indicates that SEQ ID NO: 78 and 79 are each 119 amino acids in length. However, the Sequence Listing presents SEQ ID NO: 50 as 138 amino acids and SEQ ID NO: 18 as 127 amino acids. Therefore, the lengths of the sequences in the Figure and those referred to in the Brief Description of Figure 1A do not match. If the sequences shown in Figure 1A represent partial sequences of those shown in the Sequence Listing, the specific residues represented by the partial sequences should be identified in the Figure description.

Furthermore, while the description indicates that Figure 1A depicts the HuAIP13 VH sequences of SEQ ID NO: 18, the specification teaches with respect to HuAIP13 that the "DNA sequences of the humanized VL and VH mini-exons are depicted in SEQ ID NOs: 17 and 19, and deduced amino acid sequences ... of the humanized VL and VH mini-exons [are depicted] in SEQ ID NOs: 18 and 20, respectively" (pg 34, lines 4-7). Thus, SEQ ID NO: 18 appears to be a VL sequence rather than a VH sequence.

Furthermore, the description of Figure 1A refers to "HuAIP12 T55I variant VH amino acid sequence (SEQ ID NO. 78)". However, the "T55I" sequence shown in the Figure has a threonine and not an isoleucine at position 55, and instead the threonine at position 59 has been changed to isoleucine. Furthermore, SEQ ID NO: 78 does not have an isoleucine at position 55; it has a threonine at position 55 and an isoleucine at position 59.

Therefore, the specification is objected to because the Brief Description of Figure 1A does not accurately describe the sequences shown in the Figure, and further does not correspond to the sequences present in the Sequence Listing

(5) The Brief Description of Figure 1B states that it depicts "the HuAIP12 VL amino acid sequence (SEQ ID NO. 48) and the HuAIP13 VL amino acid sequence (SEQ ID NO. 17)" (pg 4, lines 1-2). Figure 1B shows two VL sequences labeled HuAIP12 and HuAIP13, each of which is 107 amino acids. However, the Sequence Listing filed 6/1/06 indicates that SEQ ID NO: 48 is 127 amino acids in length. Furthermore, the Sequence Listing filed 6/1/06 indicates that SEQ ID NO: 17 is a not amino acid sequence, but rather a nucleic acid sequence of 412 residues. As described above, page 34 of the specification teaches that the HuAIP13 VL sequence is SEQ ID NO: 18, which is also 127 amino acids.

Therefore, the specification is objected to because the Brief Description of Figure 1A does not accurately describe the sequences shown in the Figure, and further does not correspond to the sequences present in the Sequence Listing. If the sequences shown in Figure 1B represent partial sequences of those shown in the Sequence Listing, the specific residues represented by the partial sequences should be identified in the Figure description.

(6) The disclosure is objected to because it contains an embedded hyperlink (browser-executable code). See page 9, line 16. Applicants are required to delete the embedded hyperlink. See MPEP § 608.01 (part VII).

(7) The sentence on page 34, lines 4-7 contains two typographical errors: (1) an extraneous parenthesis on line 5 ("…sequences) of the…") and (2) a missing space on line 6 ("… aredepicted …").

(8) Page 44, lines 31-33 state that "The VL and VH amino acid sequences of HuAIP13 are shown in SEQ ID NOS. 17 and 18". However, in the 6/1/06 Sequence Listing SEQ ID NO: 17 is a nucleic acid sequence of 412 residues. Furthermore, page 34, lines 4-7 (quoted above) the specification appears to indicate that HuAIP13 VL and VH sequences are SEQ ID NOs: 18 and 20.

Appropriate correction is required.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 23 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 23 depends from claim 11 and recites that the antibody "is a fully human antibody". However, the antibody of claim 11 must comprise the complete recited VH (SEQ ID NO: 78) and VL (SEQ ID NO: 48) domains. As described above, the specification teaches that SEQ ID NO: 78 and 48 are humanized VH and VL domain. Thus, each of these domains comprises a mixture of mouse and human residues. Thus, the antibody of claim 11 cannot be fully human, because it must include mouse residues. Therefore, it is unclear how the antibody of claim 23, which depends from claim 11, can be fully human and yet comprise the required mouse residues of claim 11.

Claim Rejections - 35 USC § 112, 1st paragraph, enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11-20, 22 and 23 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for

(a) An antibody or antibody fragment thereof, wherein said antibody or antibody fragment comprises the variable heavy chain amino acid sequence of SEQ ID NO: 78 and the variable light chain amino acid sequence of SEQ ID NO: 48, and wherein said antibody or antibody fragment binds to the chemokine IP-10; and

(b) A method of reducing severity of at least one symptom of an inflammatory bowel disease in a subject in need thereof, comprising administering to said subject an effective amount of an antibody or antibody fragment of (a) wherein said antibody or antibody fragment that binds to IP-10 also blocks the binding of IP-10 to the receptor CXCR3;

does not reasonably provide enablement for

(c) An antibody or antibody fragment thereof, wherein said antibody comprises a variable heavy chain amino acid sequence of SEQ ID NO: 78 and a variable light chain amino acid sequence of SEQ ID NO: 48; or

(d) An antibody or antibody fragment according to (c), wherein said antibody is conjugated to a cytotoxic agent; or

(e) A method of preventing or reducing severity of at least one symptom of an inflammatory bowel disease in a subject in need thereof, comprising administering to said subject an effective amount of an antibody or antibody fragment according to (c); or

(f) An antibody or antibody fragment according to (c), wherein said antibody is a fully human antibody.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention of independent claim 11 is an antibody or antibody fragment thereof, wherein said antibody comprises a variable heavy chain (VH) amino acid sequence of SEQ ID NO: 78 and a variable light chain (VL) amino acid sequence of SEQ ID NO: 48. Claims 12-17, 22 and 23 each depend from claim 11 and are directed to an antibody with further limitations. Claims 17-20 depend from claim 11 and are directed to a method of preventing or reducing severity of at least one symptom of an inflammatory bowel disease in a subject comprising administering an effective amount of an antibody or antibody fragment of claim 11.

The specification teaches that SEQ ID NO: 48 is a VL sequence derived from the humanized antibody HuAIP12, which in turn was derived from the mouse monoclonal

antibody AIP12, which binds to the human chemokine IP-10 (also known as CXCL10). The specification teaches that SEQ ID NO: 78 is a modified VH sequence derived from HuAIP12, with a single amino acid change at residue 55 (threonine to isoleucine). This change was based on a difference in the sequence of the VH of HuAIP12 and the VH of HuAIP13, a humanized antibody derived from the mouse monoclonal antibody AIP13, which also binds IP-10. The specification teaches that "[t]he removal of a threonine residue by substitution with isoleucine at position 55 in the VH unexpectedly increased the affinity of HuAIP12 to human IP-10. In example 9, the specification teaches that "[a]s shown in FIG. 2, HuAIP12 T55I inhibited IP-10-mediated chemotaxis of Ba/F3-CXCR3 cells more efficiently than HuAIP12, indicating that HuAIP12 T55I, which has a higher affinity to human IP-10 than HuAIP12, neutralizes the function of IP-10 more strongly than HuAIP12" (pg 49, lines 17-20).

The specification teaches that the term "antibody" (¶ 16 of the published application) refers to a protein "consisting of one or more polypeptides substantially encoded by immunoglobulin genes" including the "kappa, lambda, alpha, gamma (IgG, IgG_2, IgG_3, IgG_4), delta, epsilon and mu constant region genes, as well as the myriad immunoglobulin variable V region genes (as indicated below, there are V genes for both H-heavy- and L-light-chains)".

The specification and prior art enables the skilled artisan to make and screen antibody variants comprising the complete recited VH (SEQ ID NO: 78) and VL (SEQ ID NO: 48) and identify those that retain binding to the chemokine IP-10. However, the claims encompass variants that comprise the complete recited VH (SEQ ID NO: 78) and VL (SEQ ID NO: 48), yet do not retain binding to the chemokine IP-10. For example, scFv molecules generally consist of an entire VH and an entire VL, joined by a short linker molecule. The length and flexibility of the linker is important to allow the VH and VL molecules to form the proper configuration and allow the scFv antibody to bind to the target epitope. U.S. Patent 7,297,478 teaches, "[c]orrect folding of the VH and VL regions is crucial for retention of antigen binding capacity by the scFv. The length and sequence of the linker region are critical parameters for correct folding and biological function" (col 1, lines 52-55). Other forms of variant antibodies are subject to similar

structural constraints. Thus, a significant number of the antibody variants encompassed by the claims may not retain binding to IP-10 despite comprising the complete recited VH (SEQ ID NO: 78) and VL (SEQ ID NO: 48). However, the instant specification provides no guidance regarding the use of antibodies that comprise the complete recited VH (SEQ ID NO: 78) and VL (SEQ ID NO: 48), but lack the ability to bind IP-10. It would require undue experimentation to identify a use for such antibodies in the absence of any guidance from the instant specification.

Furthermore, the claims are directed to antibodies comprising "a variable heavy chain amino acid sequence of SEQ ID NO: 78" and "a variable light chain amino acid sequence of SEQ ID NO: 48" (emphasis added by Examiner). The use of "a" results in claims of different and much larger scope than if "the" were used (i.e., "the variable…). The recitation of "a ... sequence of SEQ ID NO: …" encompasses any sequence found within the recited sequence identifier. These sequences include short sequences as small as two amino acids in length. In other words, "a variable heavy chain amino acid sequence of SEQ ID NO: 78" encompasses any two amino acids found within SEQ ID NO: 78. In contrast, "the variable heavy chain amino acid sequence of SEQ ID NO: 78" is limited to the entirety of SEQ ID NO: 78. Furthermore, with respect to the "antibody fragment" recited in the claims, such fragments including molecules with less than either a full-length VH (SEQ ID NO: 78) and/or VL (SEQ ID NO: 48). Thus, the claims encompass antibodies including essentially any fragment of SEQ ID NO: 78 and any fragment of SEQ ID NO: 48.

However, it is well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs that provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity that is characteristic of the parent immunoglobulin. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required to produce a protein having antigen-

binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites. Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al (1982. Proc Natl Acad Sci USA. 79: 1979-83). Rudikoff et al teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function. It is unlikely that antibody fragments encompassed by the claims which may contain less than the full complement of CDRs from recited VH (SEQ ID NO: 78) and VL (SEQ ID NO: 48) will have the required binding function. Undue experimentation would be required to produce the invention commensurate with the scope of the claims from the specification alone.

Furthermore, an antibody fragment can be fragments that do not even include a single amino acid residue from SEQ ID NO: 78 or SEQ ID NO: 48, e.g., any one of the constant regions (CH1-3) or the hinge region. Such molecules include an Fc region, which can be used as described below in the section titled "Claim Rejections - 35 U.S.C. 102(b)". However, the language also reads on short fragments that are incomplete regions of the constant region of the antibody. There is no support in the specification for all of the myriad fragments which are encompassed within this language. One of skill in the art could neither expect nor predict a functioning for these fragments as broadly as is claimed. Therefore, in view of the lack of guidance in the specification and in view of the discussion above one of skill in the art would be required to perform undue experimentation in order to practice the claimed invention.

Furthermore, claim 15 depends from claim 1 and limits the recited antibody to one "wherein said antibody is conjugated to a cytotoxic agent". However, while the specification contains a brief mention of said conjugates (¶ 50 of the published application), it provides no guidance on what said antibody could be used for. The teachings of the specification are directed towards use of anti-IP-10 antibodies for treatment of inflammatory bowel disease including Crohn's disease and ulcerative colitis. The skilled artisan would predict that cytotoxic agents would harm the cells of the intestine and potentially exacerbate inflammatory symptoms. Therefore, in view of the

lack of guidance in the specification and in view of the discussion above one of skill in the art would be required to perform undue experimentation in order to practice the claimed invention.

Furthermore, claims 17-20 are directed to a method of preventing or reducing severity of at least one symptom of an inflammatory bowel disease in a subject in need thereof, comprising administering to said subject an effective amount of an antibody or antibody fragment according to claim 11. Prior to Applicants' earliest priority date (12/4/03), Singh et al (2003. Journal of Immunology. 171: 1401-1406) taught that "[f]or the first time, we demonstrate that Ab therapy directed toward IP-10 is successful at impeding IBD development" (pg 1401) and "our studies both highlight the importance of IP-10-CXCR3 interactions in CD and present a new target for immunotherapy for the treatment of colitis" (pg 1405). The relevant art further teaches that a fully human anti-IP-10 antibody has entered Phase I clinical trials for the treatment of ulcerative colitis (UC) (Kuhne et al. 2007. Journal of Immunology. 178: 131; 2 pages as printed). Kuhne teaches that IP-10 (CXCL10) is "a chemotactic cytokine for activated T cells and monocytes and plays an important role in migration of cells into sites of inflammation. The receptor for CXCL10, CXCR3, is expressed by activated T cells, eosinophils, NK, and endothelial cells. CXCL10 levels are elevated in ulcerative colitis (UC) amongst other inflammatory diseases. In preclinical animal models of UC, antibodies against CXCL10 have been shown to modify disease progression". These teachings highlight that, in addition to requiring that the antibody binds to IP-10, antibodies to be used in the claimed treatment method require an additional function: the ability to block the binding of IP-10 to the receptor CXCR3. Depending on the structure, a modified antibody that binds to IP-10 will not necessarily also inhibit binding of IP-10 to the receptor CXCR3. The specification provides a chemotaxis assay for determining whether or not an anti-IP-10 antibody also inhibits binding of IP-10 to the receptor. As described in Example 9, the ability of an antibody "to block the function of IP-10 was measured by a chemotaxis assay using a stable transfectant to a murine hematopoietic cell line Ba/F3 expressing human CXCR3" (pg 49). However, the antibodies and fragments to be used in the method of claim 17 are not limited to those that can inhibit binding of IP-10 to the

CXCR3 receptor. The instant specification does not provide any guidance on how antibodies that bind IP-10, yet fail to inhibit receptor binding, could be used to treat inflammatory bowel disease. In the absence of such guidance, it would require undue experimentation to identify a way that such antibodies could be used in the claimed treatment method.

Furthermore, the specification and prior art do not provide enablement for the full scope of treated encompassed by claim 17 and dependent claims. Specifically, the claims are directed to "preventing or reducing severity of at least one symptom of inflammatory disease". While reducing the severity of at least one symptom of inflammatory bowel disease (IBD) is enabled by the teachings of the specification and the relevant art with respect to an anti-IP10 antibody that blocks IP-10 binding to CXCR3, preventing at least one symptom of IBD is not enabled. Enablement of "prevention" requires support for administration of an agent before symptoms appear, and should result in some reduction of occurrence. A disclosure of treatment of symptomatic patients alone does not support a claim to prevention in healthy, or asymptomatic, patients. In the instant case, the relevant art provides support only for reduction in severity rather than occurrence. As shown in Table II of Singh et al (2003; cited above), "Anti-IP-10 Ab" treated mice still developed some colitis (colitis score ~2.13), which while reduced compared to untreated mice (colitis score ~6.89), was still higher than that of wild type mice without colitis. This is supported by Suzuki et al (2007. Pathology International. 57: 413-420), in which a different model of murine colitis was tested for treatment with anti-IP-10. As shown in Figure 2, treatment with anti-IP-10 reduced infiltrating cells in colitis but did not restore them to wild type levels. Further, in each study, the anti-IP-10 antibody was administered after development of colitis. The instant specification provides no working examples wherein a symptom of inflammatory bowel disease is prevented. In view of the teachings of the relevant art, and the lack of guidance in the instant specification, it would require undue experimentation to identify a way that such antibodies could be used in the claimed treatment method.

Claim 19 depends from claim 17 and recites that the antibody "inhibits at least one biological activity of IP-10". However, the only biological activity of IP-10 that is

taught by the specification is the blocking the binding of IP-10 to the CXR3 receptor (¶ 25 of the published application). Thus, this claim lacks enablement for inhibiting other biological activities of IP-10. In view of the lack of guidance in the specification and in view of the discussion above one of skill in the art would be required to perform undue experimentation in order to practice the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 11-13, 16 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Carosella et al, U.S. Patent 4,719,107, published 11/12/1988.

Claim 11 encompasses an "antibody fragment" of an antibody that "comprises a variable heavy chain amino acid sequence of SEQ ID NO: 78 or a variable light chain amino acid sequence of SEQ ID NO: 48". The instant specification teaches that IP-10 antibodies of the invention include IgG antibodies, including humanized regions where the "constant region is derived from human" (¶ 51 of the published application). Thus claim 1 encompasses IgG antibodies comprising the recited variable regions and human constant regions, and antibody fragments thereof. Such antibody fragments include Fc fragments generated from IgG antibodies by digestion with the enzyme papain. Fc fragments consist of heavy chain constant regions linked by a disulfide bond.

Carosella et al teach that "through hydrolysis with papain ... the IgG molecule yields three fragments. Two fragments each have an antibody site. These are called Fab fragments. One has no antibody site but does have a number of effector functions. This is called the Fc fragment" (column 1, lines 51-56). Digestion of a human IgG molecule taught by Carosella et al would result in an antibody fragment (Fc domain) that is structurally identical to an antibody fragment (Fc domain) producing by digesting an IgG antibody of the instant invention comprising human constant regions. Therefore, the teachings of Carosella anticipate claim 11.

Claim 12 depends from claim 11 and limits the antibody to a "monoclonal" antibody, and thus encompasses an "antibody fragment" of said monoclonal antibody. Digestion of a human IgG molecule taught by Carosella et al would result in an antibody fragment (Fc domain) that is structurally identical to an antibody fragment (Fc domain) producing by digesting a monoclonal IgG antibody of the instant invention comprising human constant regions. Therefore, the teachings of Carosella anticipate claim 12.

Claim 13 depends from claim 11 and limits the antibody to a "humanized antibody", and thus encompasses an "antibody fragment" of said humanized antibody. As described above for claim 11, the Fc fragment produced from a humanized antibody of the instant invention is structurally identical to an Fc fragment produced from a human IgG molecule taught by Carosella. Therefore, the teachings of Carosella also anticipate claim 13.

Claim 16 encompasses a pharmaceutical composition comprising an antibody fragment of claim 1 and a physiologically acceptable pharmaceutical carrier. Carosella et al further teach "immunomodulating medicine composition comprising a pharmaceutically acceptable carrier and an effective amount of, as the active ingredient, Fc fragments of human IgG" (claim 1). Therefore, the teachings of Carosella also anticipate claim 16.

Claim 22 depends from claim 11 and limits the antibody to a "chimeric antibody", and thus encompasses an "antibody fragment" of said chimeric antibody. The humanized antibodies taught by the instant specification are chimeric antibodies comprising mouse and human sequences. As described above for claim 11, the Fc fragment produced from a humanized (chimeric) antibody of the instant invention is structurally identical to an Fc fragment produced from a human IgG molecule taught by Carosella. Therefore, the teachings of Carosella also anticipate claim 22.

Note

No prior has been identified that teaches an antibody or antibody fragment comprising the variable heavy chain amino acid sequence of SEQ ID NO: 78 and the variable light chain amino acid sequence of SEQ ID NO: 48.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary C. Howard whose telephone number is 571-272-2877. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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